

Contains No CBI

D



LEGAL
Wilmington, Delaware 19898

1022 000 07 11 2 07

SAC - WILMINGTON

A

21

Certified Mail
Return Receipt Requested

No CBI

88920010611

ECHO - 92 - 12444

October 15, 1992

Document Processing Center (TS-790)
Office of Pollution Prevention and Toxics
Environmental Protection Agency
401 M Street., S.W.
Washington, D.C. 20460
Attn: Section 8(e) Coordinator (CAP Agreement)

Dear Coordinator:

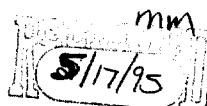
8ECAP-0025

On behalf of the Regulatee and pursuant to Unit II B.1.b. and Unit II C of the 6/28/91 CAP Agreement, E.I. Du Pont de Nemours and Co. hereby submits (*in triplicate*) the attached studies. Submission of this information is voluntary and is occasioned by unilateral changes in EPA's standard as to what EPA now considers as reportable information. Regulatee's submission of information is made solely in response to the new EPA §8(e) reporting standards and is not an admission: (1) of TSCA violation or liability; (2) that Regulatee's activities with the study compounds reasonably support a conclusion of substantial health or environmental risk or (3) that the studies themselves reasonably support a conclusion of substantial health or environmental risk.

The "Reporting Guide" creates new TSCA 8(e) reporting criteria which were not previously announced by EPA in its 1978 Statement of Interpretation and Enforcement Policy, 43 Fed Reg 11110 (March 16, 1978). The "Reporting Guide" states criteria which expands upon and conflicts with the 1978 Statement of Interpretation. Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" raises significant due process issues and clouds the appropriate reporting standard by which regulated persons can assure TSCA Section 8(e) compliance.

For Regulatee,

Mark H. Christman
Counsel
Legal D-7158
1007 Market Street
Wilmington, DE 19898
(302) 774-6443



ATTACHMENT 1

Submission of information is made under the 6/28/91 CAP Agreement, Unit II. This submission is made voluntarily and is occasioned by recent changes in EPA's TSCA §8(e) reporting standard; such changes made, for the first time in 1991 and 1992 without prior notice and in violation of Regulatee's constitutional due process rights. Regulatee's submission of information under this changed standard is not a waiver of its due process rights; an admission of TSCA violation or liability, or an admission that Regulatee's activities with the study compounds reasonably support a conclusion of substantial risk to health or to the environment. Regulatee has historically relied in good faith upon the 1978 Statement of Interpretation and Enforcement Policy criteria for determining whether study information is reportable under TSCA §8(e), 43 Fed Reg 11110 (March 16, 1978). EPA has not, to date, amended this Statement of Interpretation.

After CAP registration, EPA provided the Regulatee the June 1, 1991 "TSCA Section 8(e) Reporting Guide". This "Guide" has been further amended by EPA, EPA letter, April 10, 1992. EPA has not indicated that the "Reporting Guide" or the April 1992 amendment supersedes the 1978 Statement of Interpretation. The "Reporting Guide" and April 1992 amendment substantively lowers the Statement of Interpretation's TSCA §8(e) reporting standard². This is particularly troublesome as the "Reporting Guide" states criteria, applied retroactively, which expands upon and conflicts with the Statement of Interpretation.³ Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" and the April 1992 amendment clouds the appropriate standard by which regulated persons must assess information for purposes of TSCA §8(e).

²In sharp contrast to the Agency's 1977 and 1978 actions to soliciting public comment on the proposed and final §8(e) Policy, EPA has unilaterally pronounced §8(e) substantive reporting criteria in the 1991 Section 8(e) Guide without public notice and comment. See 42 Fed Reg 45362 (9/9/77), "Notification of Substantial Risk under Section 8(e): Proposed Guidance".

³A comparison of the 1978 Statement of Interpretation and the 1992 "Reporting Guide" is appended.

Throughout the CAP, EPA has mischaracterized the 1991 guidance as reflecting "longstanding" EPA policy concerning the standards by which toxicity information should be reviewed for purposes of §8(e) compliance. Regulatee recognizes that experience with the 1978 Statement of Interpretation may cause a review of its criteria. Regulatee supports and has no objection to the Agency's amending reporting criteria *provided that* such amendment is not applied to the regulated community in an unfair way. However, with the unilateral announcement of the CAP under the auspices of an OCM enforcement proceeding, EPA has wrought a terrific unfairness since much of the criteria EPA has espoused in the June 1991 Reporting Guide and in the Agency's April 2, 1992 amendment is new criteria which does not exist in the 1978 Statement of Interpretation and Enforcement Policy.

The following examples of new criteria contained in the "Reporting Guide" that is not contained in the Statement of Interpretation follow:

- o even though EPA expressly disclaims each "status report" as being preliminary evaluations that should not be regarded as final EPA policy or intent⁴, the "Reporting Guide" gives the "status reports" great weight as "sound and adequate basis" from which to determine mandatory reporting obligations. ("Guide" at page 20).
- o the "Reporting Guide" contains a matrix that establishes new numerical reporting "cutoff" concentrations for acute lethality information ("Guide" at p. 31). Neither this matrix nor the cutoff values therein are contained in the Statement of Interpretation. The regulated community was not made aware of these cutoff values prior to issuance of the "Reporting Guide" in June, 1991.
- o the "Reporting Guide" states new specific definitional criteria with which the Agency, for the first time, defines as 'distinguishable neurotoxicological effects'; such criteria/guidance not expressed in the 1978 Statement of Interpretation.⁵
- o the "Reporting Guide" provides new review/ reporting criteria for irritation and sensitization studies; such criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy.
- o the "Reporting Guide" publicizes certain EPA Q/A criteria issued to the Monsanto Co. in 1989 which are not in the Statement of Interpretation; have never been published in the Federal Register or distributed by the EPA to the Regulatee. Such Q/A establishes new reporting criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy.

⁴The 'status reports' address the significance, if any, of particular information reported to the Agency, rather than stating EPA's interpretation of §8(e) reporting criteria. In the infrequent instances in which the status reports contain discussion of reportability, the analysis is invariably quite limited, without substantial supporting scientific or legal rationale.

⁵ See, e.g., 10/2/91 letter from Du Pont to EPA regarding the definition of 'serious and prolonged effects' as this term may relate to transient anesthetic effects observed at lethal levels; 10/1/91 letter from the American Petroleum Institute to EPA regarding clarification of the Reporting Guide criteria.

In discharging its responsibilities, an administrative agency must give the regulated community fair and adequate warning to as what constitutes noncompliance for which penalties may be assessed.

Among the myriad applications of the due process clause is the fundamental principle that statutes and regulations which purport to govern conduct must give an adequate warning of what they command or forbid.... Even a regulation which governs purely economic or commercial activities, if its violation can engender penalties, must be so framed as to provide a constitutionally adequate warning to those whose activities are governed.

Diebold, Inc. v. Marshall, 585 F.2d 1327, 1335-36 (D.C. Cir. 1978). See also, Rollins Environmental Services (NJ) Inc. v. U.S. Environmental Protection Agency, 937 F. 2d 649 (D.C. Cir. 1991).

While neither the are rules, This principle has been applied to hold that agency 'clarification', such as the Statement of Interpretation, the "Reporting Guide" nor the April 1992 amendments will not applied retroactively.

...a federal court will not retroactively apply an unforeseeable interpretation of an administrative regulation to the detriment of a regulated party on the theory that the post hoc interpretation asserted by the Agency is generally consistent with the policies underlying the Agency's regulatory program, when the semantic meaning of the regulations, as previously drafted and construed by the appropriate agency, does not support the interpretation which that agency urges upon the court.

Standard Oil Co. v. Federal Energy Administration, 453 F. Supp. 203, 240 (N.D. Ohio 1978), aff'd sub nom. Standard Oil Co. v. Department of Energy, 596 F.2d 1029 (Em. App. 1978):

The 1978 Statement of Interpretation does not provide adequate notice of, and indeed conflicts with, the Agency's current position at §8(e) requires reporting of all 'positive' toxicological findings without regard to an assessment of their relevance to human health. In accordance with the statute, EPA's 1978 Statement of Interpretation requires the regulated community to use scientific judgment to evaluate the significance of toxicological findings and to determining whether they reasonably support a conclusion of a substantial risk. Part V of the Statement of Interpretation urges persons to consider "the fact or probability" of an effect's occurrence. Similarly, the 1978 Statement of Interpretation stresses that an animal study is reportable only when "it contains reliable evidence ascribing the effect to the chemical." 43 Fed Reg. at 11112. Moreover, EPA's Statement of Interpretation defines the substantiality of risk as a function of both the seriousness of the effect and the probability of its occurrence. 43 Fed Reg 11110 (1978). Earlier Agency interpretation also emphasized the "substantial" nature of a §8(e) determination. See 42 Fed Reg 45362, 45363

(1977). [Section 8(e) findings require "extraordinary exposure to a chemical substance...which critically imperil human health or the environment"].

The recently issued "Reporting Guide" and April 1992 Amendment guidance requires reporting beyond and inconsistent with that required by the Statement of Interpretation. Given the statute and the Statement of Interpretation's explicit focus on substantial human or environmental risk, whether a substance poses a "substantial risk" of injury requires the application of scientific judgment to the available data on a case-by-case basis.

If an overall weight-of-evidence analysis indicates that this classification is unwarranted, reporting should be unnecessary under §8(e) because the available data will not "reasonably support the conclusion" that the chemical presents a substantial risk of serious adverse consequences to human health.

Neither the legislative history of §8(e) nor the plain meaning of the statute support EPA's recent lowering of the reporting threshold that TSCA §8(e) was intended to be a sweeping information gathering mechanism. In introducing the new version of the toxic substances legislation, Representative Eckhart included for the record discussion of the specific changes from the version of H. R. 10318 reported by the Consumer Protection and Finance Subcommittee in December 1975. One of these changes was to modify the standard for reporting under §8(e). The standard in the House version was changed from "causes or contributes to an unreasonable risk" to "causes or significantly contributes to a substantial risk". This particular change was one of several made in TSCA §8 to avoid placing an undue burden on the regulated community. The final changes to focus the scope of Section 8(e) were made in the version reported by the Conference Committee.

The word "substantial" means "considerable in importance, value, degree, amount or extent". Therefore, as generally understood, a "substantial risk" is one which will affect a considerable number of people or portion of the environment, will cause serious injury and is based on reasonably sound scientific analysis or data. Support for the interpretation can be found in a similar provision in the Consumer Product Safety Act. Section 15 of the CPSA defines a "substantial product hazard" to be:

"a product defect which because of the pattern of defect, the number of defective products distributed in commerce, the severity of the risk, or otherwise, creates a substantial risk of injury to the public."

Similarly, EPA has interpreted the word 'substantial' as a quantitative measurement. Thus, a 'substantial risk' is a risk that can be quantified. See, 56 Fed Reg 32292, 32297 (7/15/91). Finally, since information pertinent to the exposure of humans or the environment to chemical substances or mixtures may be obtained by EPA through Sections 8(a) and 8(d) regardless of the degree of potential risk, §8(e) has specialized function. Consequently, information subject to §8(e) reporting should be of a type which would lead a reasonable man to conclude that some type action was required immediately to prevent injury to health or the environment.

Attachment

Comparison:

Reporting triggers found in the 1978 "Statement of Interpretation/ Enforcement Policy", 43 Fed Reg 11110 (3/16/78) and the June 1991 *Section 8(e) Guide*.

TEST TYPE	1978 POLICY CRITERIA EXIST?	New 1991 GUIDE CRITERIA EXIST?
ACUTE LETHALITY		
Oral	N}	Y}
Dermal	N}	Y}
Inhalation (Vapors)	}6	}7
aerosol	N}	Y}
dusts/ particles	N}	Y}
SKIN IRRITATION	N	Y ⁸
SKIN SENSITIZATION (ANIMALS)	N	Y ⁹
EYE IRRITATION	N	Y ¹⁰
SUBCHRONIC (ORAL/DERMAL/INHALATION)	N	Y ¹¹
REPRODUCTION STUDY	N	Y ¹²
DEVELOPMENTAL TOX	Y ¹³	Y ¹⁴

⁶43 Fed Reg at 11114, comment 14:

"This policy statements directs the reporting of specific effects when unknown to the Administrator. Many routine tests are based on a knowledge of toxicity associated with a chemical. Unknown effects occurring during such a range test may have to be reported if they are those of concern to the Agency and if the information meets the criteria set forth in Parts V and VII."

⁷Guide at pp.22, 29-31.

⁸Guide at pp.34-36.

⁹Guide at pp.34-36.

¹⁰Guide at pp.34-36.

¹¹Guide at pp.22; 36-37.

¹²Guide at pp.22

¹³43 Fed Reg at 11112

"Birth Defects" listed.

¹⁴Guide at pp.22

NEUROTOXICITY	N	Y¹⁵
CARCINOGENICITY	Y¹⁶	Y¹⁷
MUTAGENICITY		
<i>In Vitro</i>	Y}¹⁸	Y}¹⁹
<i>In Vivo</i>	Y}	Y}
ENVIRONMENTAL		
Bioaccumulation	Y}	N
Bioconcentration	Y}²⁰	N
Oct/water Part. Coeff.	Y}	N
Acute Fish	N	N
Acute Daphnia	N	N
Subchronic Fish	N	N
Subchronic Daphnia	N	N
Chronic Fish	N	N
AVIAN		
Acute	N	N
Reproductive	N	N
Reproductive	N	N

¹⁵Guide at pp-23; 33-34.

¹⁶43 Fed Reg at 11112

"Cancer" listed

¹⁷Guide at pp-21.

¹⁸43 Fed Reg at 11112; 11115 at Comment 15

"Mutagenicity" listed/ *in vivo* vs *in vitro* discussed; discussion of "Ames test".

¹⁹Guide at pp-23.

²⁰43 Fed Reg at 11112; 11115 at Comment 16.

(9)

CAS # See below for CAS No.s

Chem: 1,1,1-trichloropentafluoropropane; 1-chloro-1-bromo-2,2,3,3-tetrafluoropropane; 1,1,1-trichloro-2,2,3,3-tetrafluoropropane; 2-(w-hydro-tetrafluoroethyl)-3-trifluoromethyl-2,3,4,4-tetrafluoroacetane; 2,2,3-tris(trifluoromethyl)-3,4,4-trifluoroacetane; 2,2-bis(chlorodifluoromethyl)-3-trifluoromethyl-3,4,4-trifluoroacetane; bromomethylsulfur pentafluoride; 1,2-bis(trifluoromethyl)-1,2-bis(pentafluorosulfur)hydrazine

Title: Screening Test for anesthetic properties

Date: 2/12/63

Summary of Effects: Convulsions; unresponsiveness

Chemical CAS No.

1,1,1-trichloropentafluoropropane	4259-43-2
1-chloro-1-bromo-2,2,3,3-tetrafluoropropane	1645-78-9
1,1,1-trichloro-2,2,3,3-tetrafluoropropane	422-51-5
2-(w-hydro-tetrafluoroethyl)-3-trifluoromethyl-2,3,4,4-tetrafluoroacetane	Not known
2,2,3-tris(trifluoromethyl)-3,4,4-trifluoroacetane	Not known
2,2-bis(chlorodifluoromethyl)-3-trifluoromethyl-3,4,4-trifluoroacetane	Not known
bromomethylsulfur pentafluoride	66793-27-9
1,2-bis(trifluoromethyl)-1,2-bis(pentafluorosulfur)hydrazine	Not known

BEST COPY AVAILABLE

E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine

HASKELL LABORATORY REPORT NO. 14-63

MR NO. 656-004

Materials Tested:

1,1,1-Trichloropentafluoropropane
1-Chloro-1-bromo-2,2,3,3-tetrafluoropropane
1,1,1-Trichloro-2,2,3,3-tetrafluoropropane
2-(ω -Hydro-tetrafluoroethyl)-3-trifluoromethyl-
2,3,4,4-tetrafluorooxetane
2,2,3-Tris(trifluoromethyl)-3,4,4-trifluorooxetane
2,2-Bis(chlorodifluoromethyl)-3-trifluoromethyl-
3,4,4-trifluorooxetane
Bromomethylsulfur pentafluoride
1,2-Bis(trifluoromethyl)-1,2-bis(pentafluorosulfur)-
hydrazine

Haskell Nos.:

3359
3360
3361

3362

3363

3364

3365

3366

Submitted by: R. A. Carboni, Organic Chemicals Department
Pioneering Research Section

Other Codes: PR-218 -
225

SCREENING TEST FOR ANESTHETIC PROPERTIES

Method: Mice were exposed, two at a time, to each of a series of graded concentrations of test chemical in a 3.86 liter jar, adapted for rotation at 14 rpm. Each exposure lasted 10 minutes. Vapor concentrations were computed as percent by volume of the jar, and the required volume of liquid was injected through a rubber serum vial cap in the jar lid. In several instances, when there was a large amount of liquid to be injected, a glass wool or cotton wick was used. This wick was placed in a small spring, and attached to the vial and part directly into the jar. Also, when the amount of liquid was too large even for a wick, the material was injected in smaller doses 45 seconds apart, until the required amount had been injected into the jar. As soon as possible after injection of the test chemical, rotation of the jar was begun. The criterion of anesthesia was inability of the mouse to maintain an upright position for a minimum of 15 consecutive seconds. Mice were observed for clinical signs of toxicity for a minimum of 10 days after exposure.

BEST COPY AVAILABLE

Nominal Concentration (Volume %)	Anesthesia (+ or -)	Induction Time (min.: sec.)	Mortality Ratio	Observations
Haskell No. 3359 PR-218	1,1,1-Trichloropentafluoropropane	BP 74°C Predicted AD 50 0.3%		
4	±	4:30	2/2	During exposure: glass wool wick used. One initial struggling and falling down. One mouse convulsed and died at 2:45. Remaining mouse had consecutive but very stiff and unrelaxed rollover at 4:30. Suddenly became rigid and died at 6:30.
2	-		0/2	During exposure: slight initial incoordination; rapid respiration. After exposure: quiet, respiration slightly deep. Normal by 3:00.
Haskell No. 3360 PR-219	1-Chloro-1-bromo-2,2,3,3-tetrafluoropropane	BP 96°C Predicted AD 50 0.3%		
1	+	0:45	0/2	During exposure: initial struggling followed by relaxed rollover throughout exposure. Both mice gasping from 3:00 on. After exposure: gasping and unresponsive until 2:00 and 5:00, respectively, when respiration became more rapid and deep. One initiated activity at 5:00; one at 15:00. Gradual recovery thereafter, with both appearing normal at 31:00.
0.5	+		0/2	During exposure: initial struggling and incoordination followed by consecutive relaxed rollovers throughout exposure. Respiration deep; slight gasping in one at end of exposure. After exposure: unresponsive and respiration rapid and deep until 5:30 and 8:30, when initiated activity. Inactive until 24:00, when appeared normal.

BEST COPY AVAILABLE

Nominal Concentration (Volume %)	Anesthesia (+ or -)	Induction Time (min.: sec.)	Mortality Rate	Observations
Haskell No. 3360 (Cont'd)				
0.25	+	2:00 4:00	0/2	During exposure: initial struggling and intermittent rollover followed by consecutive, unrelaxed rollover. One appeared relaxed for about 1 minute. After exposure: inactive, rapid respiration. Seemed all right at 8:00.
				Predicted AD 50 0.3%
Haskell No. 3361 PR-220	1,1,1-Trichloro-2,2,3,3-tetrafluoropropane	BP 96°C		
1	+	1:15	0/2	During exposure: incoordination followed by consecutive rollover, which appeared relaxed at 2:00. Respiration irregular and deep; slow gasps at 3:30. Same until end. After exposure: unconscious, gasping. Rapid responsive at 7 and 8 min. Slightly responsive by 13:00. Gradual recovery by 13:00.
0.5	+	4:00	0/2	During exposure: struggling and incoordination followed by consecutive unrelaxed rollovers, with intermittent relaxation throughout exposure; respiration rapid and deep. After exposure: unconscious, rapid respiration. Activity at 1:00; appeared normal at 4:00.
0.25	+	8:00	0/2	During exposure: incoordination, rapid respiration and intermittent rollover throughout exposure. One had consecutive, but very unrelaxed rollover at 8:00. After exposure: slightly groggy, rapid respiration. Normal by 1:30.

BEST COPY AVAILABLE

Nominal Concentration (Volume %)	Anesthesia (+ or -)	Induction Time (min.: sec.)	Mortality	Observations
			Ratio	
Haskell No. 3362 PR-221	2-(ω-hydro-tetrafluoroethyl)-3-trifluoromethyl-2,3,4,4-tetrafluorooxetane	-	BP 68°C	Predicted AD 50 1-2%
4	-	0/2	During exposure: glass wool wick used. Both mice may have contacted liquid. Appeared slightly nervous at 6:00. <u>After exposure:</u> seemed normal immediately.	
2	-	0/2	No signs of toxicity or anesthesia observed, during or after exposure.	
1	-	0/2	Same as above.	
Haskell No. 3363 PR-222	2',2,3-Tris(trifluoromethyl)-3,4,4-trifluorooxetane	-	BP 51°C	Predicted AD 50 4.5%
8	-	2/2	During exposure: material injected in 4 doses at 45 sec. intervals; all injected by 2:15. Respiration slightly rapid; otherwise appeared normal throughout exposure. <u>After exposure:</u> seemed normal immediately, but both mice found dead one day later.	
6	-	2/2	Cotton wick used. Both mice may have contacted liquid. No signs of toxicity or anesthesia observed, during or immediately after exposure; however, both found dead one day later.	
4	-	2/2	Cotton wick used. Both mice may have contacted liquid. <u>During exposure:</u> one hyperactive at 2:00; <u>other</u> <u>appeared</u> <u>normal</u> . <u>After exposure:</u> normal immediately; however, both found dead one day later.	

BEST COPY AVAILABLE

Nominal Concentration (Volume %)	Anesthesia (+ or -)	Induction Time (min.: sec.)	Mortality Ratio	Observations
Haskell No. 3364 PR-223	2,2-Bis(chlorodifluoromethyl)-3-trifluoromethyl-3,4,4-trifluorooxetane	BP 109°C	Predicted AD 50 0.4%	
4	-	2/2		During exposure: material injected in 2 doses, 45 sec. apart; all injected at 0:45. Both mice appeared normal, during and immediately after exposure. However, both found dead next a.m.
2	-	2/2		No signs of anesthesia or toxicity observed, during or immediately after exposure. Both mice found dead next a.m.
1	-	2/2		Same as above.
Haskell No. 3365 PR-224	Bromomethylsulfur pentafluoride	BP 73°C	Predicted AD 50 0.6%	
1	+	0:30	0/2	During exposure: initial incoordination followed by consecutive rollovers. One relaxed at 0:30; the other relaxed at 3:00. Respiration rapid, then deep; gasping noted at 8:00.
0.75	+	0:30 1:15	0/2	During exposure: initial incoordination followed by consecutive rollovers. One relaxed at 0:30; the other relaxed at 3:00. Respiration rapid, then deep; gasping noted at 8:00.
				After exposure: unconscious and gasping. Respiration deep at 0:45 and rapid at 1:15. Responsive at 1:45 and 2:15. Gradual recovery by 5:00.

BEST COPY AVAILABLE

Nominal Concentration (Volume %)	Anesthesia (+ or -)	Induction Time (min.: sec.)	Mortality Ratio	Observations
<u>Haskell No. 3365 (Cont'd)</u>				
0.5	+	6:15 6:30	0/2	During exposure: initial incoordination and struggling followed by intermittent, then consecutive, unrelaxed rollovers; rapid respiration. After exposure: slightly groggy. Appeared normal at 2:00.
Haskell No. 3366	PR-225	1,2-Bis(trifluoromethyl)-1,2-bis (pentaffluorosulfur)-hydrazine	BP 100°C	Predicted AD 50.1-2%
6	-	-	0/2	During exposure: material injected in 3 doses at 45 sec. intervals; both mice contacted liquid. Intermittent incoordination and gasping. Lacrimation observed at 6:00 and 8:00. After exposure: inactive, gasping, lacrimation. Recovery in about 1 hour.
4	-	-	0/2	During exposure: material injected in 2 doses, 45 sec. apart; both mice may have contacted liquid. Slight incoordination at 3:00. After exposure: appeared all right immediately.
2	-	-	0/2	During exposure: slightly nervous at 5:00; all right thereafter. After exposure: appeared normal immediately.

Conclusions: On the basis of these tests, three of the above compounds are recommended for further testing as anesthetic agents: 1-Chloro-1-bromo-2,2,3,3-tetrafluoropropane (PR-219, Hask. No. 3360), 1,1,1-Trichloro-2,2,3,3-tetrafluoropropane (PR-220, Hask. No. 3361) and Bromomethylsulfur pentafluoride (PR-224, Hask. No. 3365).

BEST COPY AVAILABLE

Nominal Concentration (Volume %)	Anesthesia (+ or -)	Induction Time (min.: sec.)	Mortality Ratio	Observations		
				BP 109°C	Predicted AD 50	0.4%
Haskell No. 3364	PR-223	2,2-Bis(chlorodifluoromethyl)-3,4,4-trifluoromethyl-1-(trifluoroacetane				
4	-	2/2		During exposure: material injected in 2 doses, 45 sec. apart; all injected at 0:45. Both mice appeared normal, during and immediately after exposure. However, both found dead next a.m.		
2	-	2/2		No signs of anesthesia or toxicity observed, during or immediately after exposure. Both mice found dead next a.m.		
1	-	2/2		Same as above.		
Haskell No. 3365	PR-224	Bromomethylsulfur pentafluoride		BP 73°C	Predicted AD 50	0.6%
1	+	0:30	0/2	During exposure: initial incoordination followed by consecutive, relaxed rollovers throughout exposure. Respiration deep, then gasping from 5:00 on.		
				After exposure: unconscious and gasping. Respiration became deep and rapid at 2:00; both slightly responsive at 3:00. Recovery by 7:00.		
0.75		0:30 1:15	0/2	During exposure: initial incoordination followed by consecutive rollovers. One relaxed at 0:30; the other relaxed at 3:00. Respiration rapid, then deep; gasping noted at 8:00.		
	+	+		After exposure: unconscious and gasping. Respiration deep at 0:45 and rapid at 1:15. Responsive at 1:45 and 2:1. Gradual recovery by 5:00.		

duplicate page

BEST COPY AVAILABLE

PR-219 and PR-220 induced consecutive relaxed rollovers in mice at a concentration of 0.5%, with intermittent signs of anesthesia noted as low as 0.25%. Recovery after exposure was much more rapid with PR-220; 4 minutes as compared with 24 minutes at the 0.5% level. The respiratory impairment at a level of 1% for both compounds should be noted, however.

PR-224 has a minimum anesthetic level of 0.5% (although rollovers at this concentration were not relaxed), and rapid recovery followed exposure to all concentrations. The gasping during and immediately after exposure to 0.75 and 1% should be noted.

1,1,1-Trichloropentrafluoropropane (PR-218, Hask. No. 3359) failed to induce any anesthesia in mice at 2%, and produced convulsions and death at a concentration of 4%.

2-(ω -hydro-tetrafluoroethyl)-3-trifluoromethyl-2,3,4,4-tetrafluorooxetane (PR-221, Hask. No. 3362) failed to induce any signs of toxicity or anesthesia, even at the highest concentration tested, 4%. Higher concentrations were not advisable because of the large amounts of material involved, and hence the problem of rapid and efficient vaporization.

Both 2,2,3-Tris(trifluoromethyl)-3,4,4-trifluorooxetane (PR-222, Hask. No. 3363) and 2,2-Bis(chlorodifluoromethyl)-3-trifluoromethyl-3,4,4-trifluorooxetane (PR-223, Hask. No. 3364) not only failed to anesthetize mice at any level tested (8, 6 and 4% and 4, 2 and 1%, respectively), but also caused delayed deaths at each of these concentrations.

1,2-Bis(trifluoromethyl)-1,2-bis(pentafluorosulfur)-hydrazine (PR-225, Hask. No. 3366) produced incoordination, lacrimation and gasping in mice, but no signs of anesthesia at 6%, the highest level tested.

Report by: JANE K. WIER
Jane K. Wier

Approved by: D. B. Hood
D. B. Hood
Chief, Toxicology Section

J. Wesley Clayton
J. Wesley Clayton,
Assistant Director

JKW/mfs
Date: February 12, 1963

Triage of 8(e) Submissions

Date sent to triage: _____

NON-CAP

CAP

Submission number: 12404A

TSCA Inventory:

Y

N

D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX

SBTOX

SEN

W/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX

CTOX

EPI

RTOX

GTOX

STOX/ONCO

CTOX/ONCO

IMMUNO

CYTO

NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

For Contractor Use Only

entire document: 0 1 2 pages 1,9

pages _____

Notes:

Contractor reviewer : JW

Date: 1/17/96

✓

CAS # See below for CAS No.s

Chem: 1,1,1-trichloropentafluoropropane; 1-chloro-1-bromo-2,2,3,3-tetrafluoropropane; 1,1,1-trichloro-2,2,3,3-tetrafluoropropane; 2-(w-hydro-tetrafluoroethyl)-3-trifluoromethyl-2,3,4,4-tetrafluoroxyacetane; 2,2,3-tris(trifluoromethyl)-3,4,4-trifluoroxyacetane; 2,2-bis(chlorodifluoromethyl)-3-trifluoromethyl-3,4,4-trifluoroxyacetane; bromomethylsulfur pentafluoride; 1,2-bis(trifluoromethyl)-1,2-bis(pentafluorosulfur)hydrazine

Title: Screening Test for anesthetic properties

Date: 2/12/63

Summary of Effects: Convulsions; unresponsiveness

Chemical CAS No.

1,1,1-trichloropentafluoropropane	4259-43-2
1-chloro-1-bromo-2,2,3,3-tetrafluoropropane	1645-78-9
1,1,1-trichloro-2,2,3,3-tetrafluoropropane	422-51-5
2-(w-hydro-tetrafluoroethyl)-3-trifluoromethyl-2,3,4,4-tetrafluoroxyacetane	Not known
2,2,3-tris(trifluoromethyl)-3,4,4-trifluoroxyacetane	Not known
2,2-bis(chlorodifluoromethyl)-3-trifluoromethyl-3,4,4-trifluoroxyacetane	Not known
bromomethylsulfur pentafluoride	66793-27-9
1,2-bis(trifluoromethyl)-1,2-bis(pentafluorosulfur)hydrazine	Not known

12404A

L

1,1,1-Trichloropentafluoropropane: Acute inhalation toxicity in mice is of low concern. Single 10-minute inhalation exposures to mice (2/group) at levels of 20,000 or 40,000 ppm were lethal to 2/2 high-concentration mice. Anesthesia (inability to maintain upright position) occurred within 4½ minutes at 40,000 ppm. Clinical signs in high-concentration mice included struggling, falling, convulsions, and "consecutive but very stiff and unrelaxed rollover." Low-concentration mice exhibited slight initial incoordination and rapid respiration during exposure.

L

1-Chloro-1-bromo-2,2,3,3-tetrafluoropropane: Acute inhalation toxicity in mice is of low concern. Single 10-minute inhalation exposures to mice (2/group) at levels of 2,500, 5,000 or 10,000 ppm were not lethal. Anesthesia (inability to maintain upright position) occurred within 4 minutes at 2,500 ppm, within 2½ minutes at 5,000 ppm, and within 45 seconds at 10,000 ppm. Clinical signs included initial struggling, incoordination, relaxed/unrelaxed rollover, gasping, periodic unresponsiveness, and rapid deep respiration.

L

1,1,1-Trichloro-2,2,3,3-tetrafluoropropane: Acute inhalation toxicity in mice is of low concern. Single 10-minute inhalation exposures to mice (2/group) at levels of 2,500, 5,000 or 10,000 ppm were not lethal. Anesthesia (inability to maintain upright position) occurred within 8 minutes at 2,500 ppm, within 4 minutes at 5,000 ppm, and within 1¼ minutes at 10,000 ppm. Clinical signs included struggling, incoordination, relaxed/unrelaxed rollover, gasping, rapid deep respiration, and unconsciousness.

L

2-(ω -hydro-tetrafluoroethyl)-3-trifluoromethyl-2,3,4,4-tetrafluorooxetane: Acute inhalation toxicity in mice is of low concern. Single 10-minute inhalation exposures to mice (2/group) at levels of 10,000, 20,000 or 40,000 ppm were not lethal. No significant signs of toxicity or anesthesia occurred.

L

2,2,3-Tris(trifluoromethyl)-3,4,4-trifluorooxetane: Acute inhalation toxicity in mice is of low concern. Single 10-minute inhalation exposures to mice (2/group) at levels of 40,000, 60,000 or 80,000 ppm were lethal to all exposed mice. No significant signs of toxicity or anesthesia occurred.

L

2,2-Bis(chlorodifluoromethyl)-3-trifluoromethyl-3,4,4-trifluorooxetane: Acute inhalation toxicity in mice is of low concern. Single 10-minute inhalation exposures to mice (2/group) at levels of 10,000, 20,000 or 40,000 ppm were lethal to all exposed mice. No significant signs of toxicity or anesthesia occurred.

L

Bromomethylsulfur pentafluoride: Acute inhalation toxicity in mice is of low concern. Single 10-

minute inhalation exposures to mice (2/group) at levels of 5,000, 7,500, or 10,000 ppm were not lethal. Anesthesia (inability to maintain upright position) occurred within 6½ minutes at 5,000 ppm, within 1¼ minutes at 7,500 ppm, and within 30 seconds at 10,000 ppm. Clinical signs included incoordination, relaxed/unrelaxed rollover, gasping, rapid deep respiration, and unconsciousness.

L

1,2-Bis(trifluoromethyl)-1,2-bis(pentafluorosulfur)-hydrazine: Acute inhalation toxicity in mice is of low concern. Single 10-minute inhalation exposures to mice (2/group) at levels of 20,000, 40,000 or 60,000 ppm were not lethal. The high-concentration mice exhibited incoordination, gasping, lacrimation, and inactivity. Slight incoordination also was seen in mid-concentration mice. Anesthesia did not occur in any of the exposed mice.